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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,202	12/04/2001	Keith D. Allen	R-902	6809

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1031 Bing Street
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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 10/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,202	ALLEN, KEITH D.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,8 and 16-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,8 and 16-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

The applications cited in the specification on pg 10, line 19, and pg 11, line 1, will need updated as necessary.

Claims 1-5, 7, 9-15 and 16-24 are under consideration in the instant office action. Claim 8 is missing a label, but it is "currently amended."

Claim Rejections - 35 USC § 101

Claims 6, 8 and 16-24 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility.

Claims 6 and 16-24 are directed toward a transgenic animal having a disruption of a Kir5.1 gene, an inwardly rectifying potassium channel.

The art at the time of filing did not teach mice with a disruption in the Kir5.1 gene. However, the art at the time of filing taught mice with a disruption in GIRK2 (Kir3.2) are indistinguishable from wild-type mice, while *wv/wv* mice, having a single point mutation in the Kir3.2 gene, had extensive cerebellar granule cell death, dopaminergic neuronal loss in the substantia nigra, male infertility, and spontaneous seizures (Signorini, 1997, PNAS, Vol. 94, pg 923-927). Thus, different mutations in inwardly rectifying potassium channels caused different phenotypes. The specification teaches making Kir5.1 -/- mice having dwarfed body shape (pg 53, lines 21-22), decreased body weight, spleen weight

and spleen:body weight ratio (pg 54, lines 54), and increased startle response (pg 55, lines 8-11).

The mouse claimed does not have a specific utility. The specification suggests using the mice as a model of disease but does not disclose a specific disease in humans linked to a disruption in Kir5.1 (pg 18, lines 8-9; pg 19, lines 21-23). The specification suggests using the mice to compounds that alter a physiological response in the mice (pg 19, lines 5-20). The specification does not teach a disruption in Kir5.1 correlates to any specific disease or physiological response in humans, specifically dwarfism, decreased spleen weight, or anxiety as claimed. Using the mice claimed to identify compounds is not specific to the mouse claimed because wild-type mice may be used to identify such compounds. In fact, any mouse can be used to find compounds that increase body weight, increase spleen weight or decrease the startle response. The specification teaches the "open field test" is generic to the hearing processing, sensory and motor processing, global sensory processing and motor abnormalities (pg 54, lines 20-25) as well as sensorimotor processing, attention, anxiety and thought disturbance (pg 54, lines 26-30); therefore, the "open field test" is not specific to any disease. Thus, using the mouse claimed to identify compounds is not specific to that mouse, and the mouse claimed does not have a use that is specific to any disease in humans.

The mouse claimed does not have a substantial utility. Claims 10-11, step c) require administering compounds to the mice and determining whether Kir5.1 gene expression is modulated. Compounds that modulate Kir5.1 expression cannot be found

using the mice disclosed because Kir5.1 is not expressed in the mice. Claim 24 requires using identifying an agent that ameliorates a phenotype associated with Kir5.1 by administering compounds to the mice and determining whether a phenotype is ameliorated; however, the specification does not identify any compounds that alter physiological responses using the mice. Therefore, using the mouse to identify compounds is not substantial.

Claim 8, directed toward cells having a disrupted Kir5.1 gene, is included because the cells lack a specific and substantial utility for the reasons above.

Applicants argue knockout mice had a "well-known utility," i.e. "for further study of these disorders and their association with the Kir5.1 gene." Applicants cite MPEP 2701 II(A)(3). Applicants' arguments are not persuasive. Applicants leave out the final phrase of MPEP 2701 II(A)(3).

> If at any time during the examination, it becomes readily apparent that the claimed invention has a well-established utility, do not impose a rejection based on lack of utility. An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible. (underlining added)

Applicants' have also failed to recognize the Utility Guidelines available to the public.

> REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS repeated from http://www.uspto.gov/web/menu/utility.pdf

"Specific Utility" - A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed.

"Substantial utility" - a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material, which has a stated correlation to a predisposition to the onset of a particular disease condition, would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":

A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

B. A method of treating an unspecified disease or condition. (Note, this is in contrast to the general rule that treatments of specific diseases or conditions meet the criteria of 35 U.S.C. 101.)

C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility".

D. A method of making a material that itself has no specific, substantial, and credible utility.

E. A claim to an intermediate product for use in making a final product that has no specific, substantial, and credible utility.

(Page 5-7 of utility guidelines).

A "well-known utility" is a specific, substantial and credible utility which is well know, immediately apparent, or implied by the specification's disclosure of the properties of the material, alone or taken with the knowledge of one skilled in the art. Neither a "well-established utility" nor a "specific utility" applies to any utility that one can dream up for an invention or a utility that would apply to virtually every member of a general class of materials, such as proteins or DNA.

(Paragraph bridging pg 32-33 of utility guidelines).

It was well known to knock out a gene to determine its function or what will happen when the gene is not expressed. However, scientific "utility" is not the same as "patentable utility" or a "well-established" utility.

The MPEP and utility guidelines clearly set forth that a "well-established utility" must be specific, substantial and credible. At the time of filing, knockout mice were used for further research in the art at the time of filing. However, further research does not rise to the level of a "well-established utility" because such a utility is not substantial, specific or credible.

The utility guidelines specifically state that further research is not a "substantial utility":

> [T]he following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":
>
> A. Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved.

In this case, further study of mice would have been required to determine how to use the mouse of applicants' invention (with increased startle response, dwarfism, decrease body size, body weight or spleen weight) as a model of disease. Further study would be required to determine the function of the disrupted gene. The overall phenotype of the applicants' mice does not correlate to any disorder; therefore, further study would be required to determine

antagonists have generally failed to establish the existence of pharmacologically distinct receptor types within the $GABA_B$ receptor class. The advent of $GABA_{B1}$ knockout mice has also failed to provide support for multiple receptor types" (pg 247, col. 2, lines 4-). Thus, knockout mice may be used to identify agents that bind to the knocked out gene ($GABA_B$ in the case of Bowery or Kir5.1 in the instant application), but the agent may not treat disease or ameliorate any symptom of disease. Further research would be required to determine how to use such an agent identified using the mouse, which is not a "substantial utility" (see Utility Guidelines for examples of things that do not have "substantial utility" "C. A Method of assaying for or identifying a material that itself has no "specific and/or substantial utility"). Using the mice to identify agents capable of altering a phenotype is also not a "specific utility" because the agent may be affecting other proteins in the pathway and not Kir5.1 itself. Using the mice to identify agents capable of altering a phenotype is also not a "specific utility" because the agent may be found using wild-type mice.

Overall, the mice claimed do not have a "well-established utility" because using the mice for further research (to determine how to use the mouse as a model of non-disclosed disease, to determine the function of the gene or to identify agents capable of altering a phenotype) is not a "specific utility" or "substantial utility."

Applicants argue the mice have been ordered by at least four pharmaceutical companies; therefore, applicants conclude that those of skill

would recognize the utility of the mice. Applicants' argument is not persuasive. Sales may be evidence to overcome a 103 obviousness rejection, but there is no case law that establishes that "sales" are evidence of patentable utility. Evidence of sales is not evidence the mice have a "well-established" utility or a "specific utility" or a "credible utility."

Claim Rejections - 35 USC § 112

Claims 6, 8 and 16-24 remain also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In addition, the specification does not reasonably provide enablement for any animal, Kir5.1 gene, phenotype, cell, disruption, method of making a transgenic or method of using a transgenic as broadly claimed.

Claims 6 and 16-24 are directed toward a transgenic animal having a disruption of a Kir5.1 gene. The art at the time of filing did not teach mice with a disruption in the Kir5.1 gene. However, the art at the time of filing taught mice with a disruption in GIRK2 (Kir3.2) are indistinguishable from wild-type mice while *wv/wv* mice, having a single point mutation in the Kir3.2 gene, had extensive cerebellar granule cell death, dopaminergic neuronal loss in the substantia nigra, male infertility, and spontaneous seizures (Signorini, 1997, PNAS, Vol. 94, pg 923-927). Thus, different mutations in inwardly rectifying potassium channels caused different results.

how to use the mice to study a disorder. Thus, using the mice claimed for further research is not a "substantial utility."

Using the mice to identify the function of the knocked out gene is not a "substantial utility" or "specific utility." Olsen (GABA in the Nervous System, 2000, pg 81-95) taught that "although gene targeting is often useful in delineating the contribution of a given gene product to phenotypic characteristics observed, some gene knockouts lead to embryonic or perinatal lethality, and others lead to no apparent phenotype. This can arise from a lack of any role for the gene in question in regard to the trait studies or from compensation by other gene products. Analysis of the compensation can yield valuable clues to the genetic pathway" (pg 82, last 11 lines of col. 1). Thus, knockout mice may not be capable of elucidating the function of the protein and may only provide a clue to a pathway the protein being knocked out is involved in. using mice to obtain a clue to a pathway is not a "substantial utility." Using a mouse with a phenotype caused by genes compensating for a knocked out gene is not a "specific utility" because the phenotype is not specific to the knocked out gene.

Using the mice to identify agents capable of altering a phenotype would require further research and is not a "substantial utility" or "specific utility." Bowery (Pharm. Rev., 2002, Vol. 54, pg 247-264) taught, "no unique pharmacological or functional properties have been assigned to either subunit or the variants" of $GABA_B$. "The emergence of high-affinity antagonists for $GABA_B$ receptors has enabled a synaptic role to be established. However, than

The specification teaches making Kir5.1 -/- mice having dwarfed body shape (pg 53, lines 21-22), decreased body weight, spleen weight and spleen:body weight ratio (pg 54, lines 54), and increased startle response (pg 55, lines 8-11).

Claim 8 is included because it is a cell derived from the mouse of claim 6.

Applicants' arguments refer to the arguments provided in the 101 rejection. Applicants' arguments were addressed above and were not found persuasive.

Claim 18 remains rejected and claims 16, 19, 22 and 24 as amended are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 as newly rejected is unclear because the limitation of "further exhibits increased startle response" is actually defining how the "anxiety" in claim 6 was determined. As written, it appears that the phenotype in claim 16 is separate from the phenotypes in claim 6, but it is actually further limiting the phenotype of "anxiety" in claim 6.

Claim 18 remains indefinite because it is unclear if "further exhibits a stimulus processing disorder" further limits the anxiety in claim 6 (because anxiety was established using acoustic stimuli) or if the phrase is a limitation separate from the phenotype of "anxiety" in claim 6.

Claim 19 as newly rejected is unclear because the limitation of "further exhibits a growth disorder" is actually broader than the "dwarfism, decreased body size,

decreased body weight or decreased spleen weight" in claim 6. As written, it appears that the phenotype in claim 19 is separate from the phenotypes in claim 6, but it is actually broader than the phenotypes in claim 6, which does not further limit the claim.

Claim 22 as newly rejected is unclear because the limitation of "further exhibits a spleen abnormality" is actually broader than the "decreased spleen weight" in claim 6. As written, it appears that the phenotype in claim 22 is separate from the phenotype in claim 6, but it is actually broader than the phenotype in claim 6, which does not further limit the claim.

Claim 24 is included because it is dependent upon claim 22.

Claim Rejections - 35 USC § 103

The rejection of claims 3-9, 14 and 24 under 35 U.S.C. 103(a) as being unpatentable over Signorini (1997, PNAS, Vol. 94, pg 923-927) in view of Mouri (Genomics, 1998, Vol. 54, pg 181-182) has been withdrawn because Signorini in view of Mouri did not teach the mice would have anxiety, dwarfism, decreased body size, decreased body weight or decreased spleen weight as claimed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

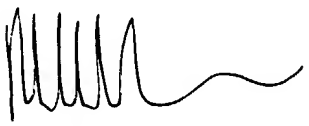
Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson



MICHAEL WILSON
PRIMARY EXAMINER